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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/038,206	01/02/2002	Jasper Rine	UOCB118456	1317

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EXAMINER

BRUSCA, JOHN S

ART UNIT PAPER NUMBER

1631

DATE MAILED: 03/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/038,206

Applicant(s)

RINE ET AL.

Examiner

John S. Brusca

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 December 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 38-85 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 38-85 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION


1. In view of the supplemental appeal brief filed on 21 December 2005, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

 3/2/06
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER

Priority

2. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. §120 as follows:

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The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent applications and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, Application Nos. 09/294453, 08/986650, and 08/512753 fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The parent applications do not describe a matrix of probes comprising a predetermined sequence of nucleotides that are hybridizable to genes, transcripts of genes, or cDNA.

Specification

3. The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

Claims 38-68 and 70-85 are drawn to methods that employ a matrix of probes comprising a predetermined sequence of nucleotides that are hybridizable to genes, transcripts of genes, or

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cDNA. The specification does not describe a matrix of probes comprising a predetermined sequence of nucleotides that are hybridizable to genes, transcripts of genes, or cDNA. On page 18 the instant specification discusses Fodor et al. as showing an example of an array of oligonucleotides on a silicon substrate. On page 19 of the instant specification a blanket statement incorporates by reference all publications cited in the specification. If the Fodor et al. publication describes the claimed matrix of probes comprising a predetermined sequence of nucleotides that are hybridizable to genes, transcripts of genes, or cDNA, then the applicants should incorporate this description as described in the previous paragraph.

4. The disclosure is objected to because of the following informalities: On page 18, line 17 the specification recites an incorrect citation for Fodor et al '91 by reciting a volume number of "251". The Fodor et al. '91 article is of record in the Information Disclosure Statement filed 20 November 2002, which correctly lists the volume number as 251.

Appropriate correction is required.

5. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claims 38-68 and 70-85 are drawn to methods that employ a matrix of probes comprising a predetermined sequence of nucleotides that are hybridizable to genes, transcripts of genes, or cDNA. The specification does not describe a matrix of probes comprising a predetermined sequence of nucleotides that are hybridizable to genes, transcripts of genes, or cDNA. The applicants are cautioned to not insert new matter into the specification.

Claim Rejections - 35 USC § 101

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6. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claim 69 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 69 is drawn to data in computer readable memory which is not patentable subject matter (see MPEP 2106).

8. Applicant's arguments in the appeal brief filed 21 December 2005 have been fully considered but they are not persuasive. The applicants state that the claim is drawn to functional descriptive material that affects the functioning of a computer. However the clause following "wherein" does not affect the content of the data in computer memory that is being claimed. It is further noted that the added clause states how a computer could use the data but does not address the position of the Office that the claimed data does not affect how a computer functions, rather the data merely is entered to a computer that is programmed to process data in a particular way and the claimed data does not affect how the computer processes the data.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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10. Claims 38-85 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to methods or data produced by a method, wherein the method uses a matrix of probes comprising a predetermined sequence of nucleotides that are hybridizable to genes, transcripts of genes, or cDNA. The specification does not describe a matrix of probes comprising a predetermined sequence of nucleotides that are hybridizable to genes, transcripts of genes, or cDNA. In particular, the specification does not describe a matrix with a predetermined sequence, or how to make such a matrix. Although the phrase “a matrix of probes comprising a predetermined sequence of nucleotides that are hybridizable to genes, transcripts of genes, or cDNA” appears in originally filed claims in the instant application, the specification makes no mention of a matrix with predetermined sequences. The specification instead focuses on using a matrix comprising polynucleotides whose sequence has not been predetermined. The specification only discusses a probe matrix on page 18 and incorporates by reference Fodor et al '91 without describing how the matrix is made or what is known about the sequence of the probes in the matrix.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 38-53, 55-66, and 68-83, and 85 are rejected under 35 U.S.C. 102(a) as being anticipated by Fodor et al. '01 (U.S. Patent No. 6,309,822).

13. Claims 38-53, 55-66, and 68-85 are rejected under 35 U.S.C. 102(e) as being anticipated by Fodor et al. '01 (U.S. Patent No. 6,309,822).

The claims are drawn to a method of assay of the response of a living thing to a stimulus by use of an array of probes comprising a predetermined sequence of nucleotides to individual gene transcripts by comparing databases comprising results of hybridizations of labeled polynucleotides derived from cells either treated with different stimuli or unstimulated control cells, the database produced by the method, and methods of generating the database produced by the method. The responses are measured by converting an output signal to an electrical signal and then converting the electrical signal to a value in a database. In some embodiments at least 50% of the gene transcripts of the cell are assayed, the cells are human cells, the probes consist of 24-240 nucleotides, and the database is computer implemented. In some embodiments the

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probes are in an X and Y coordinate grid. In some embodiments the method is repeated for different stimuli.

Fodor et al. '01 shows an array of probes to RNA transcripts in columns 2-4, and assay of expression of genes after cells are treated with drugs or other stimuli in column 5, lines 63-column 6, line 9, and column 16, lines 26-36. Fodor et al. '01 shows computer analysis and stored array hybridization level data in column 7, lines 4-34. Fodor et al. '01 shows analysis of basal levels of transcription relative to levels after stimulus in columns 5, line 34-column 6, line 9. Fodor et al. '01 shows analysis of functional classes of genes in column 16, lines 45-57. Fodor et al. '01 shows probe lengths of 5-500 bases in column 3, lines 34-39, analysis of human genes at least in column 35, lines 34-62, analysis of all 40,000 human genes for which there are EST's in column 14, lines 52-60, and synthesis of arrays resulting in locations with a designed and predetermined sequence in columns 30-33. Fodor et al. '01 shows fluorescent microscope assay of an array, and signal evaluation by computer, and storage in a computer database in columns 35-43.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 38-53, 55-66, 68-83, and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gress et al. in view of Granelli-Piperno et al. in view of either Fodor et al. '98 (U.S. Patent No. 5,800,992) or Fodor et al. '91 (reference 9 in the Information Disclosure Statement filed 20 November 2002).

The claims are drawn to a method of assay of the response of a living thing to a stimulus by use of an array of probes comprising a predetermined sequence of nucleotides to individual gene transcripts by comparing databases comprising results of hybridizations of labeled polynucleotides derived from cells either treated with different stimuli or unstimulated control cells, the database produced by the method, and methods of generating the database produced by the method. The responses are measured by converting an output signal to an electrical signal and then converting the electrical signal to a value in a database. In some embodiments at least 50% of the gene transcripts of the cell are assayed, the cells are human cells, the probes consist of 24-240 nucleotides, and the database is computer implemented. In some embodiments the

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probes are in an X and Y coordinate grid. In some embodiments the method is repeated for different stimuli.

Gress et al. shows throughout, and especially on page 609 and figure 3 a general method of assaying patterns of transcription by use of labeled cDNA from mouse, and human cells by use of a cDNA X-Y coordinate grid array of probes. The array provides an optical signal of expression in an assayed human cell of individual genes in the cell. Gress et al. shows importing the resulting data via an electrical signal of a Phosphorimager to a computer implemented relational database on page 616. Gress et al. shows in the abstract that their high density array allows for the efficient assay of thousands of clones simultaneously. Gress et al. shows on page 612 that polyA control probes hybridize non-specifically to many array cDNA probes and that other cDNA probes in the array contained repetitive sequences that also caused non-specific hybridization. Gress et al. shows on page 616 that one strategy to avoid background non-specific hybridization is to use probes that lack polyA tails by use of modified primers. Gress et al. does not show subsection of assayed cells to different stimuli, or comparison of the transcriptional profile of cells that have received different stimuli, or assay of discrete portions of the complete number of genes of the cell, or use of probes with a predetermined sequence of nucleotides.

Granelli-Piperno et al. shows in figures 1-9 the effect of a variety of compounds on expression of genes of human cells. The tested compounds include cytokines, mitogens, cyclosporin A, and cycloheximide. The response is determined by the intensity of a film image on an autoradiograph. Granelli-Piperno et al. show that assay of expression of genes after

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treatment of cells with drugs allows a determination of the effect of the drug on individual gene expression and further serves to gain insights on the mechanism of action of the drug.

Fodor et al. '98 shows throughout a method of making an array of polynucleotide probes of predetermined sequence by independent in situ stepwise synthesis of each oligonucleotide probe on the array. Fodor et al. '98 shows in columns 32, lines 12-24 that their arrays may be used to map the location of a molecule on a chromosomal map. Fodor et al. '98 shows in column 35 that their procedure may be used to assay the developmental stage cells from which the assayed sample is derived. In column 78-79, Fodor et al. '98 shows that their method may be used to assay developmental stages of cells by assay of their mRNA content.

Fodor et al. '91 shows in the abstract and pages 771-772 a method of synthesizing a dinucleotide of a predetermined sequence by a photolithographic process. Fodor et al. '91 concludes on page 772 that oligonucleotide arrays that could be made by their method would be useful to detect complementary sequences in RNA and DNA, and could be used for gene mapping, fingerprinting, and diagnostics.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Gress et al. by assaying cells that have received treatments with different drugs according to the method of Granelli-Piperno et al. because Granelli-Piperno et al. shows that such an analysis serves to gain insights on the mechanism of action of the drug. It would have been further obvious to assay additional numbers of genes as desired to determine the effect of a drug on additional genes. Regarding the size of the probes, it would have been obvious to use portions of a cDNA probe of Gress et al. because Gress et al.

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shows that many array probes suffer from non-specific hybridization due to repetitive sequences of polyA tracts and that the problem may be solved by use of shorter probes. It would have been further obvious to make and use an array of probes with a predetermined sequence made by the methods disclosed by Fodor et al. '98 or Fodor et al. '91 because Fodor et al. '98 and Fodor et al. '91 show that such an array has the advantage of allowing the sequences detected in the sample to be mapped to a particular location of the genome of the organism sampled. Regarding the limitations of claims 71 and 72, it would be further obvious to one of skill in the art to perform simple mathematical comparisons of the levels in stimulated and control cells such as subtraction or division by the basal level to reveal the extent of change in the level of the assayed mRNA.

17. Claims 38, 49-51, 54, 56, 63-65, 67, 70, 80-82, and 84 are rejected under 35

U.S.C. 103(a) as being unpatentable over Gress et al. in view of Granelli-Piperno et al. in view of either Fodor et al. '98 or Fodor et al. '91 as applied to claims 38-53, 55-66, 68-83, and 85 above, and further in view of Watson et al.

The claims are drawn to assays utilizing fungal cells.

Gress et al. in view of Granelli-Piperno et al. in view of either Fodor et al. '98 or Fodor et al. '91 as applied to claims 38-53, 55-66, 68-83, and 85 above does not show assay of fungal cells.

Watson et al. shows on pages 573-575 that yeast cells contain genes that are regulated by stimuli such as metabolites.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Gress et al. in view of Granelli-Piperno et al. in

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view of either Fodor et al. '98 or Fodor et al. '91 as applied to claims 38-53, 55-66, 68-83, and 85 above by using yeast gene probes and cells because Watson et al. shows that yeast cells have genes that are regulated by stimuli.

18. Claims 38, 49-51, 54, 56, 63-65, 67, 70, 80-82, and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fodor et al. '01 in view of Watson et al.

The claims are drawn to assays utilizing fungal cells.

Fodor et al. '01 does not show assay of fungal cells.

Watson et al. shows on pages 573-575 that yeast cells contain genes that are regulated by stimuli such as metabolites.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Fodor et al. '01 by using yeast gene probes and cells because Watson et al. shows that yeast cells have genes that are regulated by stimuli.

19. Applicant's arguments filed in the appeal brief on 21 December 2005 have been fully considered but they are not persuasive. The applicants state that Gress et al. does not need to sequence the cDNA hybridization targets and would render the array of Gress inoperable, however Gress et al. does sequence selected clones subsequent to hybridization analysis to facilitate correlation of their results with other databases as shown in the abstract of Gress et al. It is therefore apparent that the prior art shows advantages and motivation for determining the sequence of elements of an array. Fodor et al. has been cited to show that the prior art details a method to create an array with predetermined sequences at each element, which has the advantage of obviating subsequent sequencing to characterize elements of interest determined by

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the hybridization experiment. Sequencing all array elements provides additional information from hybridization of a cDNA sample to the array by showing which sequences hybridize and which sequences do not hybridize, all of which is useful for mapping regions of transcription to a genome. In addition, if all elements are initially sequenced, the probes in the array may be used for subsequent array hybridization experiments without the need for any additional sequencing of the probes in the array.

Conclusion

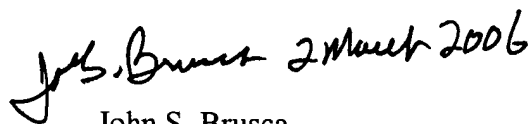
20. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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For all other customer support, please call the USPTO Call Center at (800) 786-9199. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, PhD. can be reached on 571 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Handwritten signature of John S. Brusca, dated 2 March 2006.

John S. Brusca

Primary Examiner

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jsb